Re Item I

Basis of the opinion

1. Application as filed.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: SAGATOVA F ET AL.: 'Enzymatic conversion of phosphatidylcholine to phosphatidylglcerol' APPLIED BIOCHEMISTRY AND MICROBIOLOGY, vol. 32, no. 5, 1996, pages 452-456, XP000957684 NEW YORK, NY, US ISSN: 0003-6838

   D2: ANTHONSEN T ET AL: 'Phospholipids hydrolysis in organic solvents catalysed by immobilised phospholipase C' JOURNAL OF MOLECULAR CATALYSIS B-ENZYMATIC, (4 JAN 1999) VOL. 6, NO. 1-2, PP. 125-132. PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. , XP000957601

   D3: DATABASE WPI Week 8813 Derwent Publications Ltd., London, GB; AN 1988-087107 XP002151651 'Phospholipid prodn. - by reacting a phospholipid material and a reactor substance by contacting with phospholipase D' & JP 63 036791 A (NIPPON OILS & FATS CO LTD), 17 February 1988 (1988-02-17)

2. The subject-matter of claims 1-14 appears to fulfill the requirements of Article 33 (2) and (3) PCT.

2.1 Although D1, which is considered to represent the closest prior art, discloses a method of conducting an enzyme-catalysed hydrolysis of phosphatidylcholine in a lecithin-silica gel-water system (D1 page 452, column 1, materials and methods), , wherein the enzyme used is Phospholipase D at concentrations higher than 3 mg/ml (D1, page 454, Figure 3), said document does not teach or suggest the possibility that a liposomal environment would have been beneficiary for high

scale and high conversion rate (comparing the present application and D1) from phosphatidylcholine (PC) to phosphatidyl glycerol. Furthermore, D1 discloses different ratios between PC and silica gel than the ones disclosed in the present application and, according to figure 5 of D1 a higher ratio (such as in the present application) would result in the decrease in the yield of conversion.

2.2 Both D2 and D3 disclose a method of conducting an enzyme-catalysed hydrolysis of phosphatidylcholine using silica gel (D2, page 125, abstract, D3 whole document), wherein the silica gel used is silica gel 60 from Merck, which includes mean particles of 15 µm, in D2 (D2, page 127, column 1, lines 17 and 18) and a silica gel with preferable size for mean particles between 0.02 and 0.5 mm in D3 (D3 whole document).
The enzyme used is Phospholipase C in D2 and Phospholipase D in D2 (D2, page 125, abstract, D3 whole document).
However, both documents do nor disclose or suggest a liposomal system for said conversion. Said system would allow the reaction to be performed in an aqueous environment (in both D2, page 126, column 1, lines 27 and 28, and D3, whole document, water content is reduced as small as possible) which is suitable for pharmaceutical and/or nutritional purposes whereas systems requiring the use of organic solvents for large scale conversion are often not suitable for the above mentioned purposes.

Hence, claims 1-14 of the present Application appears to fulfill the requirements of Article 33 (2) and (3) PCT.

Re Item VIII
Certain observations on the international application

1. The term "about" used in claim 5 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Attachment 7 #7

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 00/00350

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N9/16 C12P9/00 C12P13/00 C12N9/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X AA	SAGATOVA F. ET AL.: "Enzymatic conversion of phosphatidylcholine to phosphatidylglcerol" APPLIED BIOCHEMISTRY AND MICROBIOLOGY, vol. 32, no. 5, 1996, pages 452-456, XP000957684 NEW YORK, NY, US ISSN: 0003-6838 the whole document -/-	1-7,9-13

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 November 2000	15/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Oderwald, H

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 00/00350

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X AB	ANTHONSEN T ET AL: "Phospholipids hydrolysis in organic solvents catalysed by immobilised phospholipase C" JOURNAL OF MOLECULAR CATALYSIS B-ENZYMATIC, (4 JAN 1999) VOL. 6, NO. 1-2, PP. 125-132. PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. , XP000957601 the whole document	1-3,6, 11,12
X AC	RAKHIMOV M M ET AL: "PROPERTIES OF PHOSPHO LIPASE D FROM RAPHANUS-SATIVUS" BIOCHEMISTRY (ENGLISH TRANSLATION OF BIOKHIMIYA), vol. 46, no. 2 PART 1, 1981, pages 197-204, XP000953112 ISSN: 0006-2979 the whole document	1-6,9-12
X AD	DATABASE WPI Week 8813 Derwent Publications Ltd., London, GB; AN 1988-087107 XP002151651 "Phospholipid prodn. - by reacting a phospholipid material and a reactor substance by contacting with phospholipase D" & JP 63 036791 A (NIPPON OILS & FATS CO LTD), 17 February 1988 (1988-02-17) abstract	1-4,6,7
A AE	ALLGYER T T ET AL: "PHOSPHO LIPASE D EC-3.1.4.4 FROM SAVOY CABBAGE PURIFICATION AND PRELIMINARY KINETIC CHARACTERIZATION" BIOCHEMISTRY, vol. 18, no. 24, 1979, pages 5348-5353, XP002151650 ISSN: 0006-2960 cited in the application	-

2